II. REMARKS:

A. Status of the Claims

Claims 1-18 were originally filed with the case. An Office Action requesting that Applicants select a single species for examination was mailed on October 7, 2005. Applicants timely responded, electing the species of AIT-082. Another Restriction Requirement was mailed on January 26, 2006, asserting that the application claimed three patentably distinct inventions and requiring that Applicants elect an invention for examination. Applicants timely responded, electing the Group I invention, directed to a method of treating dry eye.

Claims 1-6 were rejected in the Office Action mailed May 17, 2006. In a Response to Office Action filed on November 17, 2006, claims 1, 5, and 6 were amended, claim 4 was cancelled, and claims 7-18 were withdrawn as being directed to a non-elected invention. Claims 1-3,5 and 6 were rejected in the Final Office Action mailed on March 29, 2007. No claims are amended, cancelled or added in the Response to Final Office Action filed on August 29, 2007. A Notice of Appeal was timely filed on October 1, 2007, and a Request for Continued Examination was timely filed on April 4, 2008. All claims are rejected in the non-final Office Action mailed on June 18, 2008. Claim 1 is amended herein. No claims are cancelled or added. Support to the amendment to claim 1 can be found throughout the specification, for example, at page 5, lines 21-23. Thus, claims 1-3, 5 and 6 remain pending.

B. The Claims are Patentable Over Wallace and WO 00/32197

The Action rejects all claims as being obvious over Wallace and WO 00/32197. Wallace is said to teach the use of neurotrophic factors for the treatment of a number of eye

disorders, including dry eye. The Action acknowledges that Wallace lacks a teaching of AIT-082. WO 00/32197 is said to teach that AIT-082 is a well-known neurotrophic factor. Thus, the Action asserts that it would have been obvious for a person skilled in the art to use AIT-082 for the treatment of dry eye. Applicants respectfully traverse.

Wallace appears to discuss compositions containing a neurotrophic factor and their use in the treatment of ocular disorders associated with ciliary ganglionic nerve cell degeneration. The neurotrophic factors discussed in Wallace are proteinaceous compounds characterized by having a pI in the range of 5.6 to 7.0 and a molecular weight of about 31.5 kD (Wallace, col. 2, lines 39-42). It is difficult to exploit peptide or protein molecules pharmaceutically due to bioavailability problems generally resident in the pharmaceutical administration of peptides (Spec. page 4, lines 11-13). Therefore, the methods of the present invention focus on the use of small molecule compounds that promote neuron regeneration or neurite outgrowth in a pharmaceutically acceptable vehicle to treat dry eye resulting from injury to corneal nerves. Wallace does not suggest the use of any compounds other than the proteinaceous neurotrophic factors themselves. That is, Wallace contains no suggestion to use small molecule compounds that promote neuron regeneration or neurite outgrowth would be useful in the compositions and methods described.

The Action argues that "there is no evidence of record to demonstrate that difference neurotrophic factors cannot be used for the treatment of dry eye syndrome," or that "the size of compounds with neurotrophic activity can influence their treatment ability for the treatment of dry eye." Applicants assert that the Action is missing the point of distinction. The compounds discussed in Wallace are proteins or peptides. Therefore, the difference between the compounds

used in the methods of the present invention and those discussed in Wallace is more than size alone.

The Action takes the position that it would have been obvious to combine the teachings of WO 00/32917 with the teachings of Wallace because WO 00/32917 appears to discuss the use of neurotrophic factor stimulators to treat glaucomatous neuropathy and other retinal and optic nerve head degenerative diseases. Retinal and optic nerve head degenerative diseases are disorders occurring in the back of the eye. Dry eye resulting from injury to the cornea, however, is a disorder that occurs near the front of the eye. The Action states that there is no evidence to demonstrate that the dry eye can be treated differently depending on the location and cause of such disorder. The missing link in that argument is that WO 00/32917 does not discuss the treatment of dry eye, but rather the treatment of retinal and optic nerve head degenerative diseases. The Action has not provided any reason why the skilled artisan would jump from treatment of disorders affecting the tissues of the back of the eye, which do not include dry eye, to the treatment of dry eye, which occurs at the front of the eye.

WO 00/32917 does not suggest that the compounds described therein can be used to treat disorders affecting the front of the eye, such as dry eye resulting from injury to the cornea. It is well known to the skilled artisan that, in order to deliver compounds to the eye for treatment of tissues at the back of the eye, one must typically deliver the active agent directly to the tissues at the back of the eye via intravitreal or juxtascleral injection, or the like. Most known compounds do not reach the tissues at the back of the eye via administration to the front of the eye. This is especially true of large molecules, such as proteins.

According to the Supreme Court's recent decision in *KSR International Co. v. Telefax Inc. et al.*, 550 U.S. (2007), a finding of obviousness still requires a showing that there was a reason to combine the elements of cited references. The May 3, 2007, memorandum to the patent examining corps further emphasized that the PTO examiner must "identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed. The Federal Circuit recently underscored the Supreme Court's acknowledgement of the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. *Takeda Chemical Industries, Ltd. v. Alphapharm PTY, Ltd.*, slip opinion, June 28, 2007. It is submitted that the Action has failed to provide a reason the skilled artisan would have combined the teachings of the cited references to arrive at the claimed invention.

In fact, it appears that the Action has taken the teachings of the application and combined them with the cited art in order to arrive at the obviousness determination. This amounts to an improper "hindsight reconstruction" of the invention based upon the teaching in the present application. *See In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). In *Fine*, the court explained that

> [t]o imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Fine, 5 U.S.P.Q.2d at 1600 (quoting *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 U.S.P.Q. 303, 312-13 (Fed. Cir. 1983)).

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based upon Wallace and WO 00/32917 be withdrawn.

C. Conclusion

This is submitted to be a complete response to the outstanding Final Office Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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